



otopalatodigital syndrome type 2

Otopalatodigital syndrome type 2 is a disorder involving abnormalities in skeletal development and other health problems. It is a member of a group of related conditions called otopalatodigital spectrum disorders, which also includes otopalatodigital syndrome type 1, frontometaphyseal dysplasia, and Melnick-Needles syndrome. In general, these disorders involve hearing loss caused by malformations in the tiny bones in the ears (ossicles), problems in the development of the roof of the mouth (palate), and skeletal abnormalities involving the fingers and/or toes (digits). Otopalatodigital syndrome type 2 also tends to cause problems in other areas of the body, such as the brain and heart.

People with otopalatodigital syndrome type 2 have characteristic facial features including wide-set and downward-slanting eyes; prominent brow ridges; a broad, flat nose; and a very small lower jaw and chin (micrognathia). The base of the skull may be thickened. Some people with this disorder have hearing loss. Affected individuals are usually of short stature and may have abnormalities of the fingers and toes, such as unusual curvature of the fingers (camptodactyly) and shortened or absent thumbs and big toes. They may have bowed limbs; underdeveloped, irregular ribs that may cause problems with breathing; and other abnormal or absent bones. Some may be born with an opening in the roof of the mouth (a cleft palate).

In addition to skeletal abnormalities, individuals with otopalatodigital syndrome type 2 may have developmental delay, increased fluid in the center of the brain (hydrocephalus), protrusion of the abdominal organs through the navel (omphalocele), heart defects, chest abnormalities, obstruction of the ducts between the kidneys and bladder (ureters), and, in males, opening of the urethra on the underside of the penis (hypospadias).

Males with otopalatodigital syndrome type 2 generally have much more severe signs and symptoms than do females. Males with the disorder usually do not live beyond their first year, because their underdeveloped rib cage does not allow sufficient lung expansion for breathing.

Frequency

Otopalatodigital syndrome type 2 is a rare disorder, affecting fewer than 1 in every 100,000 individuals. Its specific incidence is unknown.

Genetic Changes

Mutations in the *FLNA* gene cause otopalatodigital syndrome type 2.

The *FLNA* gene provides instructions for producing the protein filamin A, which helps build the network of protein filaments (cytoskeleton) that gives structure to cells and allows them to change shape and move. Filamin A binds to another protein called actin, and helps the actin to form the branching network of filaments that make up the cytoskeleton. Filamin A also links actin to many other proteins to perform various functions within the cell.

A small number of mutations in the *FLNA* gene have been identified in people with otopalatodigital syndrome type 2. The mutations all result in changes to the filamin A protein in the region that binds to actin. The mutations responsible for otopalatodigital syndrome type 2 are described as "gain-of-function" because they appear to enhance the activity of the filamin A protein or give the protein a new, atypical function. Researchers believe that the mutations may change the way the filamin A protein helps regulate processes involved in skeletal development, but it is not known how changes in the protein relate to the specific signs and symptoms of otopalatodigital syndrome type 2.

Inheritance Pattern

This condition is inherited in an X-linked dominant pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- cranioorodigital syndrome
- faciopalatoosseous syndrome
- FPO
- OPD syndrome, type 2
- oto-palato-digital syndrome, type II
- Taybi syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Oto-palato-digital syndrome, type II
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1844696/>

Other Diagnosis and Management Resources

- GeneReview: Otopalatodigital Spectrum Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK1393>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Bone Diseases
<https://medlineplus.gov/bonediseases.html>

Genetic and Rare Diseases Information Center

- Oto-palato-digital syndrome type 2
<https://rarediseases.info.nih.gov/diseases/5802/oto-palato-digital-syndrome-type-2>

Educational Resources

- Disease InfoSearch: Oto-palato-digital syndrome type 2
<http://www.diseaseinfosearch.org/Oto-palato-digital+syndrome+type+2/5496>
- Orphanet: Otopalatodigital syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=669

Patient Support and Advocacy Resources

- Children's Craniofacial Association
<http://www.ccakids.com/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/otopalatodigital-syndrome-type-i-and-ii/>

GeneReviews

- Otopalatodigital Spectrum Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK1393>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28otopalatodigital+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3240+days%22%5Bdp%5D>

OMIM

- OTOPALATODIGITAL SYNDROME, TYPE II
<http://omim.org/entry/304120>

Sources for This Summary

- Batra P, Ryan FS, Witherow H, Calvert ML. Distraction in a case of otopalatodigital syndrome type II. *Int J Paediatr Dent*. 2006 Jul;16(4):286-91.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16759327>
- GeneReview: Otopalatodigital Spectrum Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK1393>
- Mariño-Enríquez A, Lapunzina P, Robertson SP, Rodríguez JI. Otopalatodigital syndrome type 2 in two siblings with a novel filamin A 629G>T mutation: clinical, pathological, and molecular findings. *Am J Med Genet A*. 2007 May 15;143A(10):1120-5.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17431908>
- OMIM: OTOPALATODIGITAL SYNDROME, TYPE II
<http://omim.org/entry/304120>
- Robertson SP, Twigg SR, Sutherland-Smith AJ, Biancalana V, Gorlin RJ, Horn D, Kenwrick SJ, Kim CA, Morava E, Newbury-Ecob R, Orstavik KH, Quarrell OW, Schwartz CE, Shears DJ, Suri M, Kendrick-Jones J, Wilkie AO; OPD-spectrum Disorders Clinical Collaborative Group. Localized mutations in the gene encoding the cytoskeletal protein filamin A cause diverse malformations in humans. *Nat Genet*. 2003 Apr;33(4):487-91. Epub 2003 Mar 3.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12612583>
- Robertson SP. Otopalatodigital syndrome spectrum disorders: otopalatodigital syndrome types 1 and 2, frontometaphyseal dysplasia and Melnick-Needles syndrome. *Eur J Hum Genet*. 2007 Jan; 15(1):3-9. Epub 2006 Aug 23.
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